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A computer simulation model for cost–effectiveness analysis of mass screening for Type 2 diabetes mellitus

Tony Hsiu-Hsi Chen [a,*], Ming-Fang Yen [a], Tao-Hsin Tung [b]

[a] *Graduate Institute of Epidemiology, College of Public Health, National Taiwan University, Taipei, Taiwan, ROC*
[b] *Community Medicine Research Center and Institute of Public Health, National Yang-Ming University, Taipei, Taiwan, ROC*

Abstract

The cost–effectiveness analysis of mass screening for Type 2 diabetes mellitus (DM) was performed to elucidate whether, who and how often it should be conducted in Taiwan. A series of Markov process was developed to model the disease natural history of Type 2 DM. A hypothetical cohort with 30 000 residents aged over 30 years in Taiwan was randomly assigned to three arms of screening regimes, biennial, five-yearly and the control group. A Monteo Carol computer simulation was performed to calculate effectiveness of two screening regimes compared with the control group. Direct costs and utilities were incorporated to each corresponding state to calculate the incremental costs per life-years gained and per quality-adjusted life-years (QALYs) for biennial and five-yearly screening regimes. The incremental costs for biennial screening regime were estimated at $26 750 per life-year gained, and $17 833 per QALY. The corresponding figures for five-yearly screening regime were $10 531 per life-year gained and $17 113 per QALY. The incremental costs per life-year gained and per QALY increase with age, ranging from $17 238 for aged 30–39 years to $54 700 for aged over 70 years and from $9193 to 36 467, respectively. In conclusion, mass screening for Type 2 DM, especially in younger subjects, with 5-year inter-screening interval is cost-effective in Taiwan.

Keywords: Cost–effectiveness analysis; Type 2 diabetes mellitus; Mass screening; Markov model; Monte Carol computer simulation

1. Introduction

As the prevalence of Type 2 diabetes mellitus (DM) was estimated as 6–12% in Taiwan [1,2] and Type 2 DM, if undiagnosed before the occurrence of clinical symptoms, would lead to micro-vascular complications, macro-vascular complications, and death, it is timely to consider whether a mass screening for Type 2 DM is worthwhile. However, the efficacy of mass screening for Type 2 DM in reducing complications or deaths has never been firmly demonstrated in population-based randomized trials. The efficacy of mass screening for Type 2 DM is highly dependent on many parameters including the natural history of disease process, the performance of screening tool, and the appropriate follow-up protocol. Kuo et al. [3] estimated a 50% mortality reduction from non-insulin-dependent diabetes mellitus based on a Markov model approach. However, complications of Type 2 DM were not considered

* Corresponding author. Tel.: +886-2-23587620; fax: +886-2-23587707.
E-mail address: stony@episerv.cph.ntu.edu.tw (T.H.-H. Chen).

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in this study. From an economical viewpoint, although mass screening brings about health benefits but a slew of costs will be incurred as a result of expenditure from mass screening. Consequently, whether mass screening is cost-effective is dependent on whether health benefits can outweigh the extra cost due to mass screening. A recent study from CDC Diabetes Cost–Effectiveness Study [4] using a computer simulation model also showed the effectiveness of opportunistic screening for Type 2 DM in reducing the life-time incidence of major micro-vascular complications, which resulted in gaining both life-years and quality-adjusted life-years (QALYs). Since the major focus of this study is opportunistic screening rather than the organized mass screening for Type 2 DM that is targeted to apparently healthy subject from the community. It is uncertain whether these results or models can be directly applied to mass screening.

To the best of our knowledge, the study on economic evaluation for mass screening for Type 2 DM has not been conducted yet. In addition to whether screening for Type 2 DM is worthwhile, two questions are often asked in screening scenario. These include who should be screened and how frequently one should be screened. The purposes of this study are, therefore, to use a computer simulation model to:

1. develop the disease natural history of Type 2 DM from normal, onset of DM, the manifestation of clinical complications, and finally to death;
2. quantify the efficacy of early detection of Type 2 DM in slowing or reducing the progression of major complications based on 1;
3. evaluate the effect of inter-screening interval and age at the start of screen on slowing or reducing the progression of major complications or deaths based on 1;
4. compare the cost and effectiveness of an organized screening regime with the control group without screening; and
5. assess the cost–effectiveness of Type 2 DM screening by age-specific groups and different inter-screening interval.

2. Subjects and methods

A Markov Monte Carol simulation model was developed to evaluate the efficacy of Type 2 DM screening. The model was divided into four parts as follows.

2.1. Disease natural history model

A Markov model was developed to simulate the disease natural history of Type 2 DM from normal, onset of DM, clinical complications, and finally, to deaths. The make-up of demographic characteristics in this cohort was identical to the residents in Taiwan according to vital statistics in 1995. Life-table information was also used to adjust for competing causes of deaths while the disease natural history of DM was simulated. The incidence of Type 2 DM from normal to onset of DM was 1.1%, estimated by Kuo et al. [3]. Disease progression modules from onset of DM to complications include three parts: Retinopathy, Nephropathy, and Neuropathy. Clinical definitions of health state for three major micro-vascular complications refer to Eastman et al. [5]. Transition parameters used for simulating disease progression refer to Eastman et al. [5], Javitt at al. [6], Harris et al. [7], Klein et al. [8], Ballard et al. [9], Humphrey et al. [10], USRD [11], Dyck et al. [12], Humphrey et al. [13], and CDC–DCS group [4]. Table 1 shows the baseline estimates of these parameters. It should be noted that state transitions for three complications vary by the duration of DM. The incidence and mortality rates of cardiovascular disease, estimated from the Framingham Heart Study [14], are a function of age, sex, systolic blood pressure, total cholesterol, high-density lipid level and smoking. The distributions with respect to these variables are adjusted to represent the composition of residents in Taiwan.

2.2. Screening strategies

We assess how the above disease natural history can be altered by screening policies, including two- and five-yearly regimes. A hypothetical cohort ($N = 30\,000$) with subjects aged over 30 years

was randomly assigned to two screened arms and one control arm. The screening program lasts for 10 years. Numbers of screening rounds for two- and five-yearly regimes are six and three, respectively. Each DM case after diagnosis is followed over 30 years or until death to monitor the progression of complications or death.

2.3. Treatment effectiveness

We assume early diagnosis and treatment can control glycemic level and further reduce micro- and macro-vascular complications. We also assume such glycemic control leading to the reduction of adverse consequence varies by the duration of diabetes and types of complications. Parameters with treatment efficacy refer to Eastman et al. [5], and UKPDS [15]. These estimates were modified according to Chen et al. [16].

2.4. Cost

Direct costs estimated in this study include screening cost [17], routine treatment on glycemic control [16,18–20], treatment on micro-vascular complication [17,21–24], and treatment on macro-vascular disease [25]. Indirect costs are not considered in this study.

Table 1
Baseline values for estimates of cost–effectiveness analysis using a computer simulation model

Variable	Baseline values	References
1. Incidence of Type 2 DM	0.0107	[3]
2. Transition rates of complication		
(1) Retinopathy[a]		[6,7]
NDR → non-proliferative	0.0730	
Non-proliferative → proliferative	0.0103	
Non-proliferative → macula edema	0.1928	
Proliferative → blindness	0.0148	
Macula edema → blindness	0.0330	
(2) Nephropathy & CVD mortality		[8–11]
No nephropathy → MA	0.0267	
MA → proteinunia	0.1572	
Proteinunia → ESRD[b]	0.0042	
ESRD → CVD	0.5000	
CVD → death	0.2000	
(3) Neuropathy		[12,13]
No neuropathy → symptomatic neuropathy	0.0144	
Symptomatic neuropathy → LEA[c]	0.0280	
CVD morbidity	Logistic regression	[14]
CVD mortality rate for non-ESRD patient	0.02	
3. Cost		
(1) Screening		[17]
Fasting plasma glucose test	28	
Hemoglobin test	38	
Oral glucose tolerance test	106	
(2) Routine treatment drugs		
Drugs		[17–20]
Insulin and oral agents (duration ⩾ 10)	714 per year	
Insulin (0 < duration < 10)	513 per year	
Self-testing	222 per year	
Outpatient services insulin users	618 per year	
Case management	121 per year	
(3) Complications		[6,17,22–25]
Blindness (direct medical cost)	1997 per year	
Photocoagulation treatment	2682 (life-time)	
Eye examination	84	
Neurologic examination	130	
Renal examination	1129	
End-stage renal disease	68 131 per year	
Lower extremity amputation	31 139/op	
Cardiovascular disease	2757 per year	
4. Utility for QALYs		[17,23,26]
No Type 2 diabetes	1.00	
Screen-detected Type2 diabetes	0.95	
Blindness	0.69	
ESRD	0.61	
LEA	0.80	
Discount rate	3%	

[a] Vary by duration. The current figure represents 0–5 years.
[b] Vary by duration. The current figure represents 0–12 years.
[c] Vary by duration. The current figure represents 0–9 years.

Table 2
Cumulative incidence rate of micro-vascular complications (effectiveness) by different screening regimes

Screening regimes	Blindness	ESRD	LEA
Two-yearly	3.06% (30%)	0.19% (65%)	0.97% (33%)
Five-yearly	3.13% (28%)	0.19% (65%)	0.99% (31%)
Control group	4.37%	0.54%	1.43%

2.5. Effectiveness

Outcome measures are life-years gained and QALYs. A utility value of 1.0 is assumed for each year of life lived without diabetes. A utility value of 0.95 is assigned for subjects with DM detected by screen but without further complication. The utility values for blindness [26], ESRD [17] and LEA [23] are 0.69, 0.61 and 0.8, respectively.

2.6. Remarks

Costs and benefits are discounted at 3%, and costs are expressed in US$.

3. Results

Simulated results yield 49.40, 49.86 and 54.15 of average age at diagnosis for biennial and five-yearly screening regimes, and the control group, respectively. Table 2 shows cumulative incidence rates of micro- and macro-vascular complications by screening regimes after 30 years of follow-up.

Table 3
Cost–effectiveness analysis of mass screening for Type 2 diabetes by screening regimes

Cost & outcome	Two-yearly	Five-yearly
Increased cost due to screen (in $)	2140	1369
Life-years gained	0.08	0.08
QALYs gained	0.12	0.13
Incremental cost per additional life-years (in $)	26 750	17 113
Incremental cost per QALYs (in $)	17 833	10 531

No significant difference of reducing complications was found between two- and five-yearly regimes. Compared with the control group, preventive fractions of blindness, ESRD, and LEA due to biennial screening regime were estimated as 30, 65, and 33% respectively. The corresponding figures for five-yearly regime were 28, 65, and 31% respectively. However, there is a small difference between two screening regimes with respect to the efficacy of reducing complications.

Regarding cost–effectiveness analysis, Table 3 shows cost due to screen, life-years gained, QALYs gained, incremental cost per life-year gained and incremental cost per QALY for two screening regimes as compared with the control group. Costs due to screen for biennial and five-yearly screening regimes were calculated as $2140 and 1369, respectively. Life-years gained due to screen are 0.08 in both screen programs. QALYs gained due to screen are 0.12 and 0.13 for biennial and five-yearly screening regimes. The incremental costs for biennial screening regime were estimated at $26 750 per life-year gained, and $17 833 per QALY. The corresponding figures for five-yearly screening regime were $10 531 per life-year gained and $17 113 per QALY. Table 4 shows age-specific results of the efficacy and cost–effectiveness of five-yearly mass screening. It can be seen that although the absolute cost of screening younger cohort was larger than the older cohort, extra cost would be offset with additional life-years. Table 4 also shows the extra QALYs gained due to five-yearly screening regime decrease with age. Life-years gained in the younger cohort were approximately five times longer than those in the older cohort. The incremental costs per life-year gained for age groups 30–39, 40–49, 50–59, 60–69 and 70+ for five-yearly screening regime were estimated as $17 238, 11 400, 11 842, 18 788, and 54 700, respectively. The corresponding figures with respect to QALYs are $9193, 7600, 8881, 16 700, and 36 467, respectively.

4. Discussion

A computer simulation model was performed to assess the cost–effectiveness and the cost–util-

Table 4
Cumulative incidence rate differences of five-yearly screening regime and cost–effectiveness analysis by age groups

	30–39	40–49	50–59	60–69	70+
Blindness (%)	1.61	1.49	1.14	0.61	0.34
ESRD (%)	0.47	0.41	0.26	0.12	0.06
LEA (%)	0.59	0.55	0.40	0.16	0.05
Increased cost due to screen (in $)	1379	1368	1421	1503	1094
Life-years gained	0.08	0.12	0.12	0.08	0.02
QALYs gained	0.15	0.18	0.16	0.09	0.03
Incremental cost per additional life-year (in $)	17 238	11 400	11 842	18 788	54 700
Incremental cost per QALY (in $)	9193	7600	8881	16 700	36 467

ity analysis of mass screening for Type 2 DM that is targeted to general population by simulating the disease natural history of Type 2 DM from normal, onset of Type 2 DM, micro-vascular or macro-vascular complications and finally, to death with the incorporation of cost and utility corresponding to each state. Economic evaluation with respect to the effect of inter-screening interval on the reduction of complication is also examined. The incremental costs were estimated at $10 531 per life-year gained and $17 113 per QALY gained. Compared with the corresponding figures for breast cancer screening with mammography ($3400–83 830 per life-year gained), cervical cancer screening ($50 000 life-year gained) and hypertension screening for women aged over 20 years ($87 000), five-yearly mass screening for Type 2 DM seems cost-effective. In addition, mass screening for Type 2 DM in younger cohort is more cost-effective than in the older cohort.

In contrast to results of opportunistic screening for patients with Type 2 DM, mass screening for Type 2 DM targeted to general population is rather cost-effective. Results from CDC Diabetes Cost–Effectiveness Group showed that the incremental cost of opportunistic screening among all persons aged 25 years or older was estimated at $236 449 per life-year gained and $56 649 per QALY gained that are higher than the estimates from mass screening. The reason is that extra cost incurred in mass screening for general population is offset with life-years gained. Life-years gained and QALYs gained due to screen in our five-yearly mass screening program are 0.08 and 0.13 whereas the corresponding figures in opportunistic screening are only 0.02 and 0.08.

It should be noted that the benefit of mass screening for Type 2 DM may be underestimated in this study partly due to the benefit of early detection in reducing macro-vascular diseases was not investigated and partly due to the benefit of early detection of impaired glucose tolerance was not modeled in the disease natural history. There are several other limitations to this study. First, since indirect costs were not included in this study, it is difficult to apply the results of cost–effectiveness analysis to the perspective of society. Second, we assume glycemic control is based on complete follow-up. However, whether the logistic of follow-up can be achieved is rather skeptical. Ongoing researches should be conducted to investigate this problem. Third, the screening method used in this study is based on fasting blood sugar. However, one may assess whether glycated hemoglobin, an important indicator for glycemic control, can be used for mass screening for Type 2 DM.

In conclusion, a mathematical computer simulation model was proposed to perform the cost–effectiveness analysis of mass screening for Type 2 DM. Results show mass screening for Type 2 DM with 5-year inter-screening interval in countries with 6–12% prevalence is cost-effective as compared with opportunistic screening.

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